

Addiction Research and Theory: A Commentary on The Surgeon General's Report on Alcohol, Drugs, and Health

by

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Abstract

The Office of the Surgeon General recently produced its first Report on the consequences of alcohol and drug abuse on health, making several very laudable policy recommendations. The Report also emphasizes the importance of adequate funding for biomedical research, which is good news for both researchers and patients. However, the Report is marred by a biased viewpoint on the psychology and neurobiology of drug addiction. We highlight here four controversial issues that were depicted as facts in the Report, thereby potentially misleading non-expert readers about the current state-of-the-art understanding of the psychology and neurobiology of drug addiction. It will be important to recognize a fuller range of scientific viewpoints in addiction neuroscience to avoid amplifying this bias in the coming years.

The first ever Surgeon General's Report on the consequences of alcohol and drug abuse on health was published on November 17th, 2016 (<https://addiction.surgeongeneral.gov/>). The report draws attention to a problem of epidemic proportions, as indicated by the fact that more than 6% of the United States population has a substance use disorder and an estimated 135,000 people die prematurely every year as a consequence of drug overdose and alcohol abuse. As the Surgeon General is the leading spokesperson on matters of public health in the United States, the content of this Report deserves to be analysed in detail.

Much to commend in the Surgeon General's Report

To begin with, the Surgeon General's Report should be commended for comprehensively examining the substance use disorder problem, and making several important recommendations aimed at boosting and expanding prevention, treatment, and recovery services in order to reduce the public health consequences associated with alcohol and drug use. We particularly applaud the Report's effort to draw attention to the unfortunate stigma of addictive disorders and the special needs of different patient populations, and its call for families, educators, state and federal authorities to contribute to this effort.

In addition to making policy recommendations, the Report also emphasizes the importance of adequate funding for biomedical research, by recognizing that such research is vital to obtaining findings that can improve clinical and public health approaches to substance misuse and related disorders. This is good news for both researchers in the field of drug addiction, and for patients and their families. A large body of addiction neuroscience research during the last three decades has made major inroads into the neurobiological underpinnings of substance use disorders. But much more remains to be done, and expanding this area of research is essential for the development of novel and more effective preventive and therapeutic approaches directed at curbing substance use disorders.

A biased scientific viewpoint

However, the Report falls short in meeting its stated aim of "bringing together the best available science" regarding the psychology and neurobiology of drug addiction. The very selective choice of empirical and theoretical papers included in Chapter 2 of the Report has produced a limited – perhaps even biased – viewpoint, which primarily reflects a single addiction model, namely that known as the reward deficiency or allostasis model. While that has been a major model, it is also highly controversial, and the Report neglects alternatives that might turn out be more successful. Given that the Report provides guidelines for future neurobiological research and funding, there is a risk that this bias will be amplified in the coming years.

Below we provide a critique and commentary on four key controversial issues that were depicted as facts in the Report, thereby potentially misleading readers about the current state-of-the-art understanding of the psychology and neurobiology of drug addiction.

Addictive drugs are not the same

The first issue is that the Report seemingly endorses the notion that the reinforcing effects of all addictive drugs are essentially the same, and due to the activation of dopaminergic systems of the brain, although the available evidence does not support this claim. For example, it has been known since the early 1980s that heroin's direct reinforcing effects do not require dopamine, although dopamine may be important for opioid cue-triggered craving and relapse (Badiani *et al*, 2011; Nutt *et al*, 2015).

The Report also suggests that all addictive drugs produce similar neuroadaptations in the brains of addicts, but different drugs also produce unique neuroadaptations that are important to consider (Badiani *et al*, 2011). In fact, the exact role of dopamine in mediating the rewarding effects of the many different drugs of abuse and related neuroadaptations remains an active area of investigation, and differences continue to emerge (e.g., Becker *et al*, 2016).

Dopamine and pleasure: an out-of-date notion

A second issue concerns the nature of drug reward. The Report appears to equate the reinforcing effects of drugs (which refer to changes in the frequency of a behavioral response, as acknowledged on page 2-8) to their pleasurable/hedonic effects. Although it is often thought that positive reinforcement is associated with feelings of pleasure, many researchers believe that chief brain mechanisms underlying drug abuse are separable from those responsible for the pleasant states associated to drug use, as well as those responsible for the unpleasant states of withdrawal when drug use is halted (Berridge and Kringelbach, 2014; Robinson and Berridge 2008; Shaham *et al*, 1996).

The Report also suggests that brain dopamine release is the chief cause of drug-induced euphoria. This is a throwback to the out-of-date notion that dopamine is the brain's 'pleasure transmitter', a notion that still holds sway in the popular media but it has been largely debunked in the scientific literature (Berridge and Kringelbach, 2014). For example, on page 2-19, it is stated: "Opioids attach to opioid receptors in the brain, which leads to a release of dopamine in the nucleus accumbens, causing euphoria (the high)", even though it has repeatedly been shown that the 'high' produced by heroin or by heroin-paired cues is not associated with alterations in dopaminergic transmission in the dorsal or ventral striatum (Nutt *et al*, 2015).

Stress, CRF, and addiction: a target failure

The Report focuses much attention on the importance of stress in the development of drug addiction and great prominence is given to the role of the stress neurohormone, corticotropin releasing factor (CRF), as the brain mechanism of drug withdrawal distress and cause of excessive drug use and relapse. There is little doubt that exposure to acute or chronic stress plays a significant role in drug addiction and relapse (Badiani *et al*, 2011; Shaham *et al*, 1996). Furthermore, studies using animal models have demonstrated a critical role of CRF in stress-induced drug seeking (Badiani *et al*, 2011; Shaham *et al*, 1996),

leading to the hypothesis that CRF plays a key role for in drug and alcohol dependence (Heilig and Koob, 2007). Yet, to date all attempts at developing CRF-based therapies for human addiction (or other psychiatric disorders) have been unsuccessful (Schwandt *et al*, 2016; Shaham and de Wit 2016) and major pharmaceutical companies have uniformly abandoned their development programs aimed at this target. The fact that no reference to the known failures in targeting this mechanism was made in the Report provides the readers with an unbalanced picture of the state of research in this area.

Addiction in theory

Finally, not only does the Report focus on shared neurobiological underpinnings of short- and long-term drug effects but it also endorses a particular unitary theoretical model of addiction championed by one of the Science Editors (the three-stage hedonic allostasis or reward deficit model described on pages 2-6 to 2-18). A reader of the Report not familiar with the relevant literature may be surprised to learn that only some researchers subscribe to the hedonic allostasis theory. Many others do not concur with this view and support different theoretical accounts of addiction built around processes such as aberrant learning, impaired executive (inhibitory) control over behavior and incentive-sensitization to drug use and drug cues (e.g., Robinson and Berridge, 2008; Everitt and Robbins, 2016). These alternative views are major live topics in addiction neuroscience today, but receive short-shrift in the Report.

Other researchers question altogether the explanatory value of unified addiction theories cutting across drug classes, because they do not easily reconcile with the well-known differences among opiate, psychostimulant, and alcohol abuse in terms of epidemiology, personality traits, neurobiological mechanisms, drug-induced brain neuroadaptations, and therapeutic approaches (Badiani *et al*, 2011; Nutt *et al*, 2015).

Conclusions

We recognize that a scientific mission statement requires a certain degree of simplification to be effective. Still, the scientific perspective of the Surgeon General's Report is too narrow and too limited in depth to achieve its presumed aims.

In the age of personalized medicine, a 'one-size-fits-all' approach in clinical addiction medicine, requires reconsideration. Propagating an out-of-date view that all addictive drugs are the same in producing pleasure by activating the "brain reward systems" is counterproductive in that context (even if there might be some convergence or overlap in brain mechanisms of addiction). Furthermore, no attempt at simplification should ignore the fundamental role played by genetic, sex-related, and environmental factors when it comes to the ability of commonly used drugs to activate dopaminergic circuitry (Badiani *et al*, 2011).

Also counterproductive is the attempt at enforcing the notion that there is a substantial agreement in the field concerning the theoretical framework informing addiction research.

The truth is that there are competing theories and only time will tell which of them (if any) has been more useful in leading to a better understanding of the psychology and neurobiology of drug addiction and to more effective therapies.

It will be important for such points to be recognized to ensure that the Report's authoritative nature does not bias the direction of future neurobiological research.

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